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     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
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L1          1215 S LDL AND PROTEASE?
L2             6 S L1 AND TAIL?
L3             4 DUPLICATE REMOVE L2 (2 DUPLICATES REMOVED)
L4           435 S LDL AND PROTEOLYSIS?
L5           163 DUPLICATE REMOVE L4 (272 DUPLICATES REMOVED)
L6            46 S L5 AND PROTEASE?
L7            46 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L8             2 S L7 AND TAIL?
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L10           12 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

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L5 ANSWER 17 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
AN 1998:484174 BIOSIS
DN PREV199800484174
TI **Presenilin**-1 mutations associated with familial Alzheimer's disease do not disrupt protein transport from the endoplasmic reticulum to the Golgi apparatus.
AU Tan, Yizheng; Hong, Jin; Doan, Tam; McConlogue, Lisa; Maltese, William A. (1)
CS (1) Hood Res. Program, Weis Cent. Res., Pa. State Univ. Coll. Med., 100 N. Academy Ave., Danville, PA 17822-2616 USA
SO Biochimica et Biophysica Acta, (July 1, 1998) Vol. 1407, No. 1, pp. 69-78. ISSN: 0006-3002.
DT Article
LA English
AB Mutations in genes encoding **presenilin**-1 (PS1) and **presenilin**-2 (PS2) have been linked to familial forms of Alzheimer's disease (AD). Cells expressing mutant **presenilins** produce elevated levels of Abeta42, the major amyloid peptide found in AD plaques. The mechanism whereby this occurs remains unknown, but the localization of **presenilins** to endoplasmic reticulum (ER) and Golgi compartments has suggested that they may function in intracellular trafficking pathways involved in processing beta-amyloid precursor proteins (APP). To test this possibility, we coexpressed PS1(wt), PS1(M146L), or PS1(L286V) in HEK293 cells together with the **LDL receptor**, a classic glycoprotein marker-that undergoes posttranslational O-glycosylation in the Golgi compartment. Pulse-chase analysis of the **receptor** indicated that mutant **presenilins** had no effect on ER fwdarw Golgi transport. Similar results were obtained when the studies were carried out with cells expressing the Swedish variant of APP (SWAPP751) instead of the **LDL receptor**. Moreover, secretion of the soluble exodomain polypeptide fragments of SWAPP751 that arise from alpha-secretase and beta-secretase cleavage was not markedly affected by the PS1 mutants. Despite the lack of discernible effect of the PS1 mutants on trafficking of proteins through the Golgi apparatus, they caused a substantial increase in the proportion of Abeta42 relative to total AP in the culture medium. The results suggest that mutant forms of PS1 cause elevated production of Abeta42 by a mechanism that is independent of a major disruption of exocytic trafficking of APP.
CC Nervous System - Pathology *20506
Cytology and Cytochemistry - Human *02508
Genetics and Cytogenetics - Human *03508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
BC Hominidae 86215
IT Major Concepts
Genetics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
endoplasmic reticulum; Golgi apparatus
IT Diseases
familial Alzheimer's disease: genetic disease, nervous system disease
IT Chemicals & Biochemicals
beta-amyloid precursor protein; **presenilin**-1: mutation; **presenilin**-2: mutation
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
HEK293 (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:414226 CAPLUS
DN 137:182782
TI Proteolytic processing of low density lipoprotein receptor-related protein mediates regulated release of its intracellular domain
AU May, Petra; Reddy, Y. Krishna; Herz, Joachim
CS Department of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA
SO Journal of Biological Chemistry (2002), 277(21), 18736-18743
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB The low d. lipoprotein (**LDL**) **receptor**-related protein (LRP) is a multifunctional cell surface receptor that interacts through its cytoplasmic **tail** with adaptor and scaffold proteins that participate in cellular signaling. Its extracellular domain, like that of the signaling receptor Notch and of amyloid precursor protein (APP), is proteolytically processed at multiple positions. This similarity led us to investigate whether LRP, like APP and Notch, might also be cleaved at a third, intramembranous or cytoplasmic site, resulting in the release of its intracellular domain. Using independent exptl. approaches we demonstrate that the cytoplasmic domain is released by a .gamma.-secretase-like activity and that this event is modulated by protein kinase C. Furthermore, cytoplasmic adaptor proteins that bind to the LRP **tail** affect the subcellular localization of the free intracellular domain and may regulate putative signaling functions. Finally, we show that the degrdn. of the free **tail** fragment is mediated by the proteasome. These findings suggest a novel role for the intracellular domain of LRP that may involve the subcellular translocation of preassembled signaling complexes from the plasma membrane.
ST LRP **proteolysis** secretase kinase C membrane signaling
IT Biological transport
(intracellular; proteolytic processing of low d. lipoprotein receptor-related protein mediates regulated release of its intracellular domain)
IT Cell membrane
Protein degradation
(proteolytic processing of low d. lipoprotein receptor-related protein mediates regulated release of its intracellular domain)
IT Receptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(.alpha.2-macroglobulin; proteolytic processing of low d. lipoprotein receptor-related protein mediates regulated release of its intracellular domain)
IT 338454-52-7, .gamma.-Secretase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteolytic processing of LRP by .gamma.-secretase-like activity mediates regulated release of its intracellular domain)
IT 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteolytic processing of low d. lipoprotein receptor-related protein is modulated by protein kinase C)
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Artavanis-Tsakonas, S; Science 1999, V284, P770 CAPLUS
(2) Blaumueller, C; Cell 1997, V90, P281 CAPLUS
(3) Borg, J; Mol Cell Biol 1996, V16, P6229 CAPLUS
(4) Bressler, S; Hum Mol Genet 1996, V5, P1589 CAPLUS
(5) Brou, C; Mol Cell 2000, V5, P207 CAPLUS
(6) Cao, X; Science 2001, V293, P115 CAPLUS
(7) Cupers, P; J Neurochem 2001, V78, P1168 CAPLUS

(8) de Strooper, B; Nature 1999, V398, P518 CAPLUS
(9) Dovey, H; J Neurochem 2001, V76, P173 CAPLUS
(10) Duilio, A; Nucleic Acids Res 1991, V19, P5269 CAPLUS
(11) Esler, W; Science 2001, V293, P1449 CAPLUS
(12) Fiore, F; J Biol Chem 1995, V270, P30853 CAPLUS
(13) Gotthardt, M; J Biol Chem 2000, V275, P25616 CAPLUS
(14) Guenette, S; Proc Natl Acad Sci U S A 1996, V93, P10832 CAPLUS
(15) Herz, J; Cell 1992, V71, P411 CAPLUS
(16) Herz, J; EMBO J 1988, V7, P4119 CAPLUS
(17) Herz, J; J Biol Chem 1991, V266, P21232 CAPLUS
(18) Herz, J; J Clin Invest 2001, V108, P779 CAPLUS
(19) Herz, J; Neuron 2001, V29, P571 CAPLUS
(20) Howell, B; Genes Dev 1999, V13, P643 CAPLUS
(21) Kim, S; J Biol Chem 2001, V276, P43343 CAPLUS
(22) Kimberly, W; J Biol Chem 2001, V276, P40288 CAPLUS
(23) Kinoshita, A; J Neurosci 2001, V21, P8354 CAPLUS
(24) Kounnas, M; Cell 1995, V82, P331 CAPLUS
(25) Lecourtois, M; Curr Biol 1998, V8, P771 CAPLUS
(26) Lin, S; Nat Cell Biol 2001, V3, P802 CAPLUS
(27) Liu, C; J Biol Chem 2001, V276, P28889 CAPLUS
(28) Logeat, F; Proc Natl Acad Sci U S A 1998, V95, P8108 CAPLUS
(29) Minopoli, G; J Biol Chem 2001, V276, P6545 MEDLINE
(30) Mumm, J; Mol Cell 2000, V5, P197 CAPLUS
(31) Ni, C; Science 2001, V25, P25
(32) Quinn, K; Exp Cell Res 1999, V251, P433 CAPLUS
(33) Quinn, K; J Biol Chem 1997, V272, P23946 CAPLUS
(34) Rio, C; J Biol Chem 2000, V275, P10379 CAPLUS
(35) Sakai, J; Cell 1996, V85, P1037 CAPLUS
(36) Sastre, M; EMBO Rep 2001, V2, P835 CAPLUS
(37) Shearman, M; Biochemistry 2000, V39, P8698 CAPLUS
(38) Steiner, D; Curr Opin Chem Biol 1998, V2, P31 CAPLUS
(39) Struhl, G; Cell 1998, V93, P649 CAPLUS
(40) Struhl, G; Mol Cell 2000, V6, P625 CAPLUS
(41) Trommsdorff, M; Cell 1999, V97, P689 CAPLUS
(42) Trommsdorff, M; J Biol Chem 1998, V273, P33556 CAPLUS
(43) Ulery, P; J Biol Chem 2000, V275, P7410 CAPLUS
(44) van Uden, E; Mol Cell Neurosci 1999, V14, P129 CAPLUS
(45) Willnow, T; Biochem J 1996, V313, P71 CAPLUS
(46) Willnow, T; J Cell Sci 1994, V107, P719 CAPLUS
(47) Willnow, T; Nat Cell Biol 1999, V1, PE157 CAPLUS

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=> d his

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